ISSN 1070-3632, Russian Journal of General Chemistry, 2018, Vol. 88, No. 10, pp. 2223–2226. © Pleiades Publishing, Ltd., 2018.
Original Russian Text © K.O. Khrapova, P.A. Volkov, N.I. Ivanova, A.A. Telezhkin, N.K. Gusarova, B.A. Trofimov, 2018, published in Zhurnal Obshchei Khimii, 2018, Vol. 88, No. 10, pp. 1739–1742.

LETTERS TO THE EDITOR

Chemoselective Cross-Coupling of Secondary Phosphine Chalcogenides with Aminophenols: Synthesis of Aminophenylchalcogenophosphinic Acids *O*-Esters

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Received July 5, 2018

Abstract—Chemoselective reaction of secondary phosphine chalcogenides with 2-aminophenol under mild conditions (room temperature, 2–4 h, CCl_4–Et_3N) led to the formation of aminophenylchalcogenophosphinic acids *O*-esters in a yield of up to 80%.

Keywords: secondary phosphine chalcogenides, aminophenols, chemoselective oxidative cross-coupling

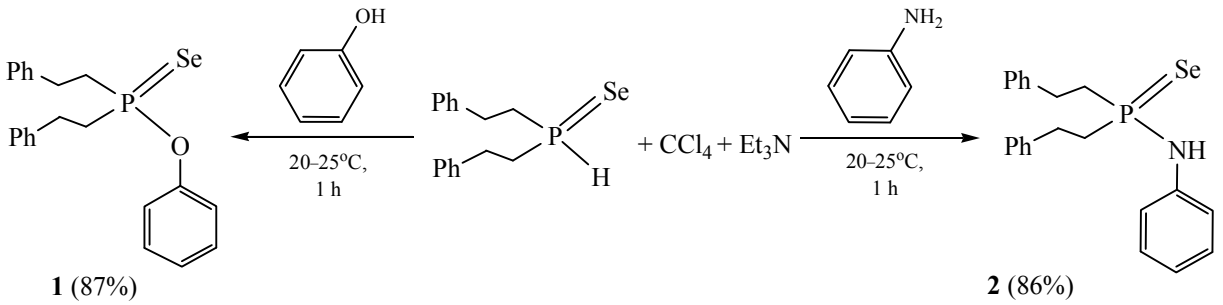
DOI: 10.1134/S1070363218100341

Oxidative cross-coupling reactions of secondary phosphine chalcogenides with NH-, OH- and SH-compounds in the presence of an oxidizing agent (CCl_4) [1] is a convenient approach to the synthesis of amides [2–4], esters [5] and thioesters [6] of chalcogenophosphinic acids, precursors of drugs [7–11], ligands for metal complex catalysts of a new generation [12–14], and intermediates for the production of modern innovative materials [15–17]. One of the promising areas of development of these reactions is the study of their chemoselectivity in the presence of two or more competing protogenic sites. Typically these are multifunctional compounds containing several HN, HO, and HS groups in various combinations. These studies open the way to new promising derivatives of phosphinic acids.

The purpose of this work was to study the reaction of secondary phosphine chalcogenides with aminophenols in the CCl_4–Et_3N system. We have previously found that phenol [5] and aniline [4] react with secondary phosphine selenides under mild conditions (room temperature, 1 h, CCl_4–Et_3N) to form ester **1** or amide **2** of selenophosphinic acid, respectively, in a yield of 86–87% (Scheme 1). Chloroform and triethylammonium hydrochloride were also identified in the reaction mixtures.

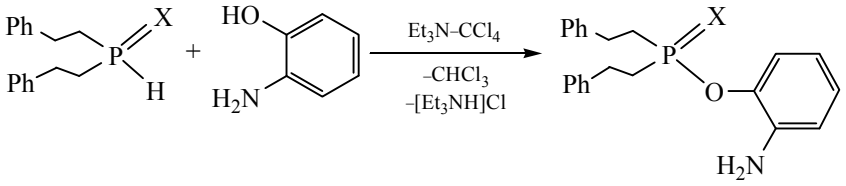
Using available (obtained from red phosphorus and styrene [18]) bis(2-phenylethyl)phosphine oxide **3a**, phosphine sulfide **3b** and phosphine selenide **3c**, as well as 2-aminophenol **4**, we showed for the first time that the oxidative cross-coupling of secondary phos-

Scheme 1.



1 (87%) **2** (86%)

Scheme 2.



3a–3c **5a–5c** (59–80%)

X = O, S, Se.

phine chalcogenides with aminophenols occurred in CCl_4–Et_3N system at room temperature in 2–4 h with the chemoselective formation of *O*-esters of aminophenylchalcogenophosphinic acids **5a–5c** in 59–80% yield (Scheme 2).

Full conversion of secondary phosphine chalcogenides **3a–3c** was achieved in 4, 3, and 2 h, respectively, i.e., their reactivity increases in the series: phosphine oxide **3a** < phosphine sulfide **3b** < phosphine selenide **3c**, which is consistent with known data [19]. As side compounds in these processes the corresponding bis(2-phenylethyl)phosphinic, -thiophosphinic and -selenophosphinic acid anhydrides were formed (detected by ^{31}P NMR using authentic samples as reference [20]). In addition, preliminary results were obtained (to be published later) that the reaction between bis(2-phenylethyl)phosphine selenide and 3-aminophenol proceeded under similar conditions (20–25°C, 7 h, CCl_4–Et_3N) also to form chemoselectively *O*-(3-aminophenyl) bis(2-phenylethyl)phosphinoselenoate.

The plausible mechanism of oxidative cross-coupling involves the formation of halide **A** in the first stage [4], which then reacts with 2-aminophenol chemoselectively involving of the hydroxyl group of the latter (Scheme 3).

The almost complete inactivity of the amino group in this process can apparently be ascribed to the well-known existence of a hydrogen bond between the hydroxyl substituent and the nitrogen atom in 2-aminophenol [21], which greatly reduces the basicity (and nucleophilicity) of the amino group.

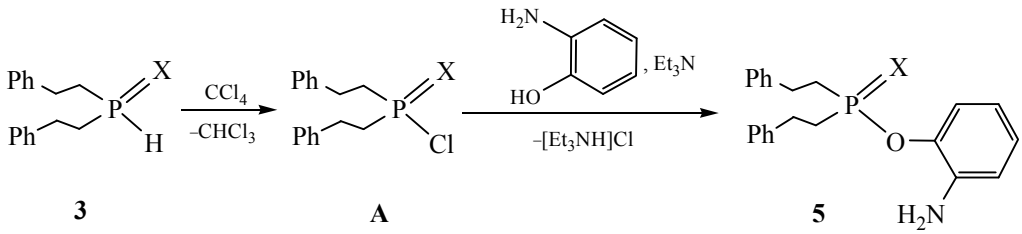
In summary, the oxidative cross-coupling of secondary phosphine chalcogenides with aminophenols easily proceeds under mild conditions (room temperature, 2–4 h, CCl_4–Et_3N system) with the chemoselective formation of *O*-esters of aminophenylchalcogenophosphinic acids.

The reactions were carried out in an inert atmosphere (argon). The reaction progress was monitored by ^{31}P NMR method.

Cross-coupling reactions of secondary phosphine chalcogenides 3a–3c with 2-aminophenol 4. To a solution of the secondary phosphine chalcogenide **3a–3c** (1.0 mmol) in a mixture of CCl_4 (3 mL) and 1,4-dioxane (1 mL) was added Et_3N (1.0 mmol). The resulting mixture was stirred at 20–25°C for 10 min, then 2-aminophenol **4** (1.0 mmol) was added and stirring continued at room temperature (20–25°C) for 2–4 h. The solvent was evaporated at a reduced pressure, 1,4-dioxane (3 mL) was added to the residue. The precipitate (triethylammonium hydrochloride) was removed by filtration, the filtrate was evaporated. The viscous residue was washed with hexane (7 × 2 mL) and dried at a reduced pressure.

2-Aminophenyl bis(2-phenylethyl)phosphinate (5a). Yield 219 mg (60%), viscous liquid. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.87–2.00 m (4H, CH_2P),

Scheme 3.



3 **A** **5**

2.80–2.92 m (4H, $PhCH_2$), 6.71–7.01 m (3H, $H^{3–5}$, OPh), 7.09–7.11 m, 7.14–7.16 m and 7.19–7.21 m (11H, Ph + H^6, OPh). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 28.4 ($PhCH_2$), 31.5 d (CH_2P, $^1J_{PC}$ = 89.5 Hz), 116.9 (C^3, OPh), 119.6 (C^5, OPh), 121.8 (C^6, OPh), 123.9 (C^4, OPh), 126.1 (C^p), 128.0 (C^o), 128.5 (C^m), 138.0 d (C^1, OPh, $^2J_{PC}$ = 6.5 Hz), 140.6 d (C^2, OPh, $^3J_{PC}$ = 3.4 Hz), 141.6 d (C^{ipso}, $^3J_{PC}$ = 14.0 Hz). ^{31}P NMR spectrum ($CDCl_3$): δ_P 56.2 ppm. Found, %: C 72.56; H 6.73; N 3.76; P 8.25. $C_{22}H_{24}NO_2P$. Calculated, %: C 72.31; H 6.62; N 3.83; P 8.48.

***O*-(2-Aminophenyl) bis(2-phenylethyl)phosphinothioate (5b).** Yield 225 mg (59%), viscous liquid. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.36–2.54 m (4H, CH_2P), 2.92–3.11 m (4H, $PhCH_2$), 6.73 d. d (1H, H^5, OPh, $^3J_{5–4} \approx {}^3J_{5–6}$ = 7.7 Hz), 6.80 d (1H, H^3, OPh, $^3J_{HH}$ = 7.7 Hz), 7.01 d. d (1H, H^4, OPh, $^3J_{4–3} \approx {}^3J_{4–5}$ = 7.7 Hz), 7.18–7.20 m, 7.22–7.26 m and 7.30–7.33 m (11H, Ph + H^6, OPh). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 29.1 d ($PhCH_2$, $^2J_{PC}$ = 2.8 Hz), 36.4 d (CH_2P, $^1J_{PC}$ = 65.0 Hz), 117.4 (C^3, OPh), 118.8 (C^5, OPh), 121.9 (C^6, OPh), 126.0 (C^4, OPh), 126.7 (C^p), 128.4 (C^o), 128.8 (C^m), 138.7 d (C^1, OPh, $^2J_{PC}$ = 10.1 Hz), 139.2 d (C^2, OPh, $^3J_{PC}$ = 3.5 Hz), 140.4 d (C^{ipso}, $^3J_{PC}$ = 15.5 Hz). ^{31}P NMR spectrum ($CDCl_3$): δ_P 105.2 ppm. Found, %: C 69.39; H 6.42; N 3.58; P 8.01; S 8.26. $C_{22}H_{24}NOPS$. Calculated, %: C 69.27; H 6.34; N 3.67; P 8.12; S 8.41.

***O*-(2-Aminophenyl) bis(2-phenylethyl)phosphinoselenoate (5c).** Yield 343 mg (80%), viscous liquid. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.48–2.64 m (4H, CH_2P), 2.94–3.11 m (4H, $PhCH_2$), 3.88 br. s (2H, NH_2), 6.71 d. d (1H, H^5, OPh, $^3J_{5–4} \approx {}^3J_{5–6}$ = 7.6 Hz), 6.78 d (1H, H^3, OPh, $^3J_{HH}$ = 7.6 Hz), 7.00 d. d (1H, H^4, OPh, $^3J_{4–3} \approx {}^3J_{4–5}$ = 7.6 Hz), 7.18–7.20 m, 7.23–7.25 m and 7.29–7.32 m (11H, Ph + H^6, OPh). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 29.6 ($PhCH_2$), 37.7 d (CH_2P, $^1J_{PC}$ = 54.7 Hz), 117.4 (C^3, OPh), 118.6 (C^5, OPh), 121.8 d (C^6, OPh, $^3J_{PC}$ = 3.4 Hz), 126.0 (C^4, OPh), 126.7 (C^p), 128.4 (C^o), 128.8 (C^m), 138.8 d (C^1, OPh, $^2J_{PC}$ = 10.3 Hz), 139.2 d (C^2, OPh, $^3J_{PC}$ = 3.4 Hz), 140.1 d (C^{ipso}, $^3J_{PC}$ = 15.9 Hz). ^{15}N NMR spectrum ($CDCl_3$): δ_N –330.0 ppm. ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 105.7 (+ satellite doublet with $^1J_{PSe}$ = 798.0 Hz). ^{77}Se NMR spectrum ($CDCl_3$), δ_{Se}, ppm: –239.5 d ($^1J_{PSe}$ = 798.0 Hz). Found, %: C 61.84; H 5.78; N 3.21; P 7.06; Se 18.25. $C_{22}H_{24}NOPSe$. Calculated, %: C 61.68; H 5.65; N 3.27; P 7.23; Se 18.43.

^1H, ^{13}C, ^{15}N, ^{31}P, and ^{77}Se NMR spectra were recorded on a Bruker DPX-400 and Bruker AV-400 spectrometers (400.13, 100.62, 40.56, 161.98, and 76.31 MHz, respectively) using HMDS (^1H, ^{13}C), $MeNO_2$ (^{15}N), Me_2Se (^{77}Se) as internal reference and 85% H_3PO_4 (^{31}P) as external reference. The signal assignment in the ^1H NMR spectra was carried out using the 2D homonuclear COSY correlation method. The signals of carbon atoms were assigned basing on the analysis of the 2D heteronuclear HSQC and HMBC correlation methods.

ACKNOWLEDGMENTS

This work was supported by the Russian Foundation for Basic Research (grant no. 18-33-00120 mol_a) using the equipment of the Baikal Analytical Center for Joint Use of the Siberian Branch of the Russian Academy of Sciences.

CONFLICT OF INTERESTS

No conflict of interests was declared by the authors.

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